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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,033	CAO ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-57 and 62-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-57 and 62-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on July 13, 2010 is acknowledged and has been entered. Claims 44-48 have been amended. Claims 1-43, 58-61 have been canceled. Claims 66-68 have been added. Claims 44-57 and 62-68 are pending.

Claims 44-57 and 62-68 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL as necessitated by Amendment.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 13, 2010 was filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. The correction of the references to GenBank entries noted as lacking dates in the submission of November 3, 2006 is acknowledged.

Claim Interpretation

The term "with specificity" is being given the broadest reasonable interpretation in light of the specification. The term is not explicitly defined in the specification. Instead, the term is

referred to in general terms such as "The specificity of a particular compound's effect on untranslated region-dependent expression of one or more other genes (preferably, a plurality of genes) can also be determined utilizing assays well-known to one of skill in the art or described herein" (p. 35, paragraph 254). Therefore, the term is being interpreted as reading on any degree of modulation of expression mediated by the VEGF UTR.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44, 50-52, 54-55, 56 and 64-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Claffey et al. (Mol Biol Cell, 1998, vol. 9, 469-481). Claffey teaches analysis of portions of the 5' and 3' UTR of the VEGF gene which modulate expression at the mRNA and protein levels (Abstract).

With regard to claim 44, Claffey teaches a method for identifying a compound that modulates human vascular endothelial growth factor (VEGF) mRNA translation governed by the untranslated regions of the human VEGF mRNA, said method comprising:

(a) contacting a compound with a human cell engineered to express a reporter protein encoded by a reporter mRNA operably linked to the full-length 5' UTR and the full-length 3' UTR of the human VEGF mRNA (Figure 3, where the VEGF 5' UTR is linked upstream of the coding

region of VEGF 3' UTR is linked downstream of the coding region; Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions); and

(b) detecting the level of the reporter protein expressed, wherein an alteration in the level of the reporter protein expressed in the presence of a compound compared to the level of the reporter protein expressed in the absence of the compound or the presence of a negative control indicates that the compound modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

With regard to claim 50, Claffey teaches an embodiment of claim 44, wherein the 5' UTR is operably linked upstream of the reporter mRNA encoding the reporter protein (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region).

With regard to claim 51, Claffey teaches an embodiment of claim 44, wherein the 3' UTR is operably linked downstream of the reporter mRNA encoding the reporter protein (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region).

With regard to claim 52, Claffey teaches an embodiment of claim 44 and 60, wherein the reporter protein is firefly luciferase, renilla luciferase, click beetle luciferase, green fluorescent protein, yellow fluorescent protein, red fluorescent protein, cyan fluorescent protein, blue fluorescent protein, beta-galactosidase, beta-glucoronidase, beta-lactamase, chloramphenicol

acetyltransferase, or alkaline phosphatase (Figure 7, where in one embodiment, the reporter construct includes the coding sequence of luciferase).

With regard to claim 54, Claffey teaches an embodiment of claim 44, wherein the human cell is engineered to transiently express the reporter protein (Figure 7 legend, where the construct was transiently transfected).

With regard to claim 55, Claffey teaches an embodiment of claim 44 or 45, further comprising measuring the effect of the compound on the level of expression of the human VEGf protein (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

With regard to claim 64, Claffey teaches an embodiment of claim 44 or 45, wherein the alteration in the level of the reporter protein expressed is detected by measuring the activity of the reporter protein (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

With regard to claim 65, Claffey teaches an embodiment of claim 44 or 45, wherein the alteration in the level of the reporter protein expressed is detected by measuring the activity of the reporter protein (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

With regard to claim 66, Claffey teaches an embodiment of claim 44 or 45, wherein the level of expression of the reporter protein in the presence of the compound is reduced relative to the level of expression of the reporter protein in the absence of the compound or the presence of the negative control (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions and where the level of

secretion/expression of the VEGF protein is decreased after increased exposure of the samples to hypoxic conditions).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45, 50-52, 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claffey et al. (Mol Biol Cell, 1998, vol. 9, 469-481) as applied to claims 44, 50-52, 54-55, 56 and 64-65 above and further in view of Levy et al. (Journal of Biological Chemistry, 1998, vol. 273, no. 11, p. 6417-6423). Claffey teaches analysis of portions of the 5' and 3' UTR of the VEGF gene which modulate expression at the mRNA and protein levels (Abstract).

With regard to claim 45, Claffey teaches a method for identifying a compound that modulates mRNA translation governed by the untranslated regions of the human VEGF mRNA said method comprising:

(a) contacting a compound with mixture expressing a reporter protein encoded by a reporter mRNA operably linked to the full-length 5' UTR and the full-3' UTR of the human VEGF mRNA (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region; Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions); and

(b) detecting the level of the reporter protein expressed, wherein an alteration in the level of the reporter protein expressed in the presence of a compound compared to the level of the reporter protein expressed in the absence of the compound or the presence of a negative control indicates that the compound modulates UTR-dependent expression of human VEGF protein (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

With regard to claim 50, Claffey teaches an embodiment of claim 45, wherein the 5' UTR is operably linked upstream of the reporter mRNA encoding the reporter protein (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region).

With regard to claim 51, Claffey teaches an embodiment of claim 45, wherein the 3' UTR is operably linked downstream of the reporter mRNA encoding the reporter protein (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region).

With regard to claim 52, Claffey teaches an embodiment of claim 45, wherein the reporter protein is firefly luciferase, renilla luciferase, click beetle luciferase, green fluorescent protein, yellow fluorescent protein, red fluorescent protein, cyan fluorescent protein, blue fluorescent protein, beta-galactosidase, beta-glucoronidase, beta-lactamase, chloramphenicol acetyltransferase, or alkaline phosphatase (Figure 7, where in one embodiment, the reporter construct includes the coding sequence of luciferase).

With regard to claim 54, Claffey teaches an embodiment of claim 45, wherein the human cell is engineered to transiently express the reporter protein (Figure 7 legend, where the construct was transiently transfected).

Regarding claim 45, Claffey does not teach contacting the cell with a cell-free translation mixture. Regarding claim 55, Claffey does not specifically teach a step of measuring the effect of the compound on the expression of human VEGF.

With regard to claim 45, Levy teaches contacting the cell with a cell-free translation mixture (p. 6418, col. 2, where cell free extracts from 293T clones were analyzed with HuR affinity purified antiserum).

With regard to claim 55, Levy teaches an embodiment of claim 45, further comprising measuring the effect of the compound on the level of expression of the human VEGF protein (Figure 5 and 6, where the Western blot shows expression analysis of the VEGF gene).

With regard to claim 56, Levy teaches an embodiment of claim 45, wherein the human cell is a HeLa cell or a 293 cell (p. 6418, col. 2, where cell free extracts from 293T clones were analyzed with HuR affinity purified antiserum).

With regard to claim 57, Levy teaches an embodiment of claim 45, wherein the cell-free translation mixture is a cell extract derived from a human cell, a yeast cell, a mouse cell, a rat cell, a Chinese hamster ovary ("CHO") cell, a Xenopus oocyte, a primary cell, an undifferentiated cancer cell, or a rye embryo (p. 6418, col. 2, where cell free extracts from 293T clones were analyzed with HuR affinity purified antiserum and where 293T is a human cell).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have applied the additional VEGF targets to the reporter gene construct

format described by Claffey. Levy teaches an analysis of the hypoxic stabilization of VEGF in the presence of an RNA binding protein, HuR, however, the inclusion of this format in the analysis of the control of the hypoxic stabilization, including the analysis of binding sites for the HuR protein would mesh well with the techniques described generally by Claffey.

Claims 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claffey et al. (Mol Biol Cell, 1998, vol. 9, 469-481) as applied to claims 44, 50-52, 54-55, 56 and 64-65 above and further in view of Stein et al. (Molec. Cell Biol., 1998, 18(6):3112-3119). Claffey teaches analysis of portions of the 5' and 3' UTR of the VEGF gene which modulate expression at the mRNA and protein levels (Abstract).

With regard to claim 46, Claffey teaches a method for identifying a compound that modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA, said method comprising:

(a) contacting a compound with a first human cell engineered to express a first reporter protein encoded by a first reporter mRNA operably linked to the full length 5' UTR and the full length 3' UTR of the human VEGF mRNA (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region; Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions); and

(c) detecting the level of expression of the first reporter protein, wherein an alteration in the level of expression of the first reporter protein in the presence of the compound relative to the level of expression of the first reporter protein in the absence of the compound or the presence of a

negative control indicates that the compound modulates human VEGF mRNA translation governed by the untranslated region of the human VEGF mRNA (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

With regard to claim 47, Claffey teaches a method for identifying a compound that t specifically modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA, said method comprising:

(a) contacting a compound with a first human cell engineered to express a first reporter protein encoded by a first reporter mRNA operably linked to the full-length 5' UTR and the full-length 3' UTR of the human VEGF mRNA (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region; Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions); and

(c) detecting the level of expression of the first reporter protein, wherein a compound that modulates human VEGF mRNA translation governed by the untranslated region of the human VEGF mRNA is identified if the level of expression of the first reporter protein in the presence of the compound is altered relative to the level of expression of the first reporter protein by the first human cell in the absence of the compound or the presence of a negative control (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

Regarding claims 46-47, Claffey does not teach the step of comparing the VEGF 5' UTR to another mRNA with a 5' and 3' UTR.

With regard to claim 46-47, Stein teaches (b) contacting the compound with a panel of human cells, wherein each human cell in the panel is isolated from each other and each human cell is engineered to express a reporter protein encoded by a reporter mRNA operably linked to a 5' UTR and a 3' UTR of a mRNA other than the human VEGF mRNA (p. 3115, Figure 3, where the reporter was operably linked to UTR of BiP mRNA instead of VEGF) and (c) detecting the level of expression of either the second reporter protein (p. 3115, Figure 3, where the levels of LUC or SeAP were measured with VEGF UTR construct and compared to constructs including the BiP UTRs in either hypoxic or non-hypoxic conditions), and no alteration in or not a substantially altered level of expression of the second or each isolated reporter protein in the panel in the presence of the compound relative to the level of expression of each isolated reporter protein in the panel in the absence of the compound or the presence of a negative control (p. 3115, Figure 3, where the levels of LUC or SeAP were measured with VEGF UTR construct and compared to constructs including the BiP UTRs in either hypoxic or non-hypoxic conditions).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Claffey to include the step of including an additional control, including the 5' and 3' UTR regulatory regions from a different gene as taught by Stein to arrive at the claimed invention with a reasonable expectation for success. As taught by Stein, "a comparison was made with the well-characterized cellular IRES contained in the 5'UTR of BiP mRNA (24)." and Stein notes "As shown in Fig. 3B, the VEGF IRES was fivefold more efficient than the BiP IRES in directing SeAP production". Stein also teaches the analysis of the reporter levels in hypoxic and non-hypoxic conditions. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have

adjusted the teachings of Claffey to include the step of including an additional control, including the 5' and 3' UTR regulatory regions from a different gene as taught by Stein to arrive at the claimed invention with a reasonable expectation for success.

Claims 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Claffey et al. (Mol Biol Cell, 1998, vol. 9, 469-481) in view of Levy et al. (Journal of Biological Chemistry, 1998, vol. 273, no. 11, p. 6417-6423) as applied to claims 46-47 above and further in view of Stein et al. (Molec. Cell Biol., 1998, 18(6):3112-3119). Claffey teaches analysis of portions of the 5' and 3' UTR of the VEGF gene which modulate expression at the mRNA and protein levels (Abstract).

With regard to claim 48, Claffey teaches a method for identifying a compound that modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA, said method comprising:

(a) contacting a compound with a cell-free translation mixture expressing a first reporter protein encoded by a first reporter mRNA operably linked to the full-length 5' UTR and the full-length 3' UTR of the human VEGF mRNA (Figure 3, where the VEGF 5' UTR is linked upstream of the coding region of VEGF 3' UTR is linked downstream of the coding region; Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions);

(c) detecting the level of expression of the first reporter proteins, wherein an alteration in the level of expression of the first reporter protein in the presence of the compound relative to the level of expression of the first reporter protein in the absence of the compound or the presence of

a negative control, indicates that a compound modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA (Figure 1C, where the effect of the UTR modulation is measured by analysis of the level of secreted protein in the presence of hypoxic conditions).

Regarding claim 48, neither Claffey nor Levy teach (b) contacting the compound with a translation mixture expressing a second reporter protein encoded by a second reporter mRNA operably linked to a 5' UTR and a 3' UTR of a mRNA other than the human VEGF mRNA; and (c) detecting the level of expression of the second reporter proteins, and no alteration in or not a substantially altered level of expression of the second reporter protein in the presence of the compound relative to the level of expression of the second reporter protein in the absence of the compound or the presence of the negative control indicates that the compound modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA.

With regard to claim 48, Stein teaches a method comprising (b) contacting the compound with a translation mixture expressing a second reporter protein encoded by a second reporter mRNA operably linked to a 5' UTR and a 3' UTR of a mRNA other than the human VEGF mRNA (p. 3115, Figure 3, where the reporter was operably linked to UTR of BiP mRNA instead of VEGF); and

(c) detecting the level of expression of the second reporter proteins, and no alteration in or not a substantially altered level of expression of the second reporter protein in the presence of the compound relative to the level of expression of the second reporter protein in the absence of the compound or the presence of the negative control indicates that the compound modulates human VEGF mRNA translation governed by the untranslated regions of the human VEGF mRNA (p.

3115, Figure 3, where the levels of LUC or SeAP were measured with VEGF UTR construct and compared to constructs including the BiP UTRs in either hypoxic or non-hypoxic conditions).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Claffey and Levy to include the step of including an additional control, including the 5' and 3' UTR regulatory regions from a different gene as taught by Stein to arrive at the claimed invention with a reasonable expectation for success. As taught by Stein, "a comparison was made with the well-characterized cellular IRES contained in the 5'UTR of BiP mRNA (24)." and Stein notes "As shown in Fig. 3B, the VEGF IRES was fivefold more efficient than the BiP IRES in directing SeAP production". Stein also teaches the analysis of the reporter levels in hypoxic and non-hypoxic conditions. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have adjusted the teachings of Claffey and Levy to include the step of including an additional control, including the 5' and 3' UTR regulatory regions from a different gene as taught by Stein to arrive at the claimed invention with a reasonable expectation for success.

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Claffey et al. (Mol Biol Cell, 1998, vol. 9, 469-481) as applied to claims 44, 50-52, 54-55, 56, 58-59 and 64-65 and further in view of Benjamin et al. (PNAS, 1997, vol. 94, p. 8761-8766). Claffey teaches analysis of portions of the 5' and 3' UTR of the VEGF gene which modulate expression at the mRNA and protein levels (Abstract).

With regard to claim 53, Benjamin teaches an embodiment of claim 44, wherein the human cell is engineered to stably express the reporter protein (p. 8761, col. 2, 'preparation and

analysis of pTET-VEGF cell lines' heading, where glioma cells were stably transfected with pTET-VEGF construct).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of stable transfection of a VEGF reporter construct as taught by Benjamin into the method of VEGF protein secretion analysis as taught by Claffey to arrive at the claimed invention with a reasonable expectation for success. As taught by Benjamin, "C6 glioma cells were cotransfected with pTET-VEGF, pTET-TAK and a plasmid encoding G418 resistance. Following stable selection in G418, colonies were picked, amplified and tested for tetracycline-regulated expression of VEGF" (p. 8761, col. 2). Therefore, considering that the method of forming stable cell lines was known at the time the invention was made, it would have been obvious to one of ordinary skill in the art to have applied the method of stable transfection of a VEGF reporter construct as taught by Benjamin into the method of VEGF protein secretion analysis as taught by Claffey to arrive at the claimed invention with a reasonable expectation for success.

Claims 49 and 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claffey et al. (Mol Biol Cell, 1998, vol. 9, 469-481) as applied to claims 45, 50-52, 54-57 above and further in view of Hyder et al. (Cancer Research. 2000, vol. 60, p. 3183-3190) and Cho et al. (Expert Opin Ther Targets, 2002, vol. 6, no. 6, p. 679-689).

Claffey teaches analysis of portions of the 5' and 3' UTR of the VEGF gene which modulate expression at the mRNA and protein levels in the presence of hypoxia. However, this compound does not have a specific structure (Abstract).

Levy also teaches analysis of elements in the 5' and 3' UTR of the VEGF gene which modulate expression following estrogen response.

With regard to claim 49, Levy teaches an embodiment of claim 45, wherein the compound does not alter VEGF mRNA levels (see Figures 5 and 6, where the mRNA was stabilized in the presence of HuR).

With regard to claim 64-65, Levy teaches an embodiment of claim 44 or 45, wherein the alteration in the level of the reporter protein expressed is detected by measuring the activity of the reporter protein (Figure 5 and 6, where the Western blot shows expression analysis of the VEGF gene).

Regarding claims 62-63, Claffey or Levy do not teach determining the structure of the compound.

With regard to claim 62, Cho teaches an embodiment of claim 44 or 45 further comprising (c) determining the structure of the compound (Figure 8, where in a library where the small molecule comprises a protein, the structure can be determined using mass spectrometry).

With regard to claim 63, Cho teaches an embodiment of claim 62, wherein the structure of the compound is determined by mass spectroscopy, NMR, vibrational spectroscopy, or X-ray crystallography (Figure 8, where in a library where the small molecule comprises a protein, the structure can be determined using mass spectrometry).

It would have been prima facie obvious to one of ordinary skill to include a rationally designed target library in the screening for compounds which modulate expression of VEGF, particularly as controlled or mediated by the 5' or 3' UTR of the VEGF gene. Cho teaches "proteomics analyzes differentially regulated proteins, elucidates protein structure and function,

and indentifies interacting partners" (p. 684). Cho also teaches "the most common method in proteome analysis is to perform a 2D gel electrophoresis (2-DE) on a protein sample preparation isolated from a defined set of conditions (i.e. normal versus diseased and control versus drug-treated). Protein bands of interest are digested and identified using mass spectrometry (See Figure 8)" (p. 686). Therefore, it would have been obvious to one of ordinary skill to include a rationally designed target library in the screening for compounds which modulate expression of VEGF, particularly as controlled or mediated by the 5' or 3' UTR of the VEGF gene.

Conclusion

No claims are allowed. All claims stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephanie K. Mummert/
Primary Examiner, Art Unit 1637

SKM